



LabLink

Laboratory Information from the Michigan Department of
Community Health Bureau of Laboratories

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From the Laboratory Director

Frances Pouch Downes, Dr. P.H.

In December, 1999 the Centers for Disease Control and Prevention (CDC) published a list of 10 great public health accomplishments, 1900-1999 (see page 2). This list provides an opportunity to review the role of the public health laboratory in these accomplishments. It also identifies current and future challenges for public health laboratories.

Leading causes of death in the early part of the century were pneumonia, influenza, tuberculosis and gastroenteritis. The sources, or associations, of these disease patterns were grounded in poor hygiene and poor sanitation. Additionally, poor nutrition, poor maternal and infant health and unsafe work places defined health risks.

Throughout the first half of the twentieth century, the new science of microbiology produced technology which made control of some of the most common infectious diseases a possibility. The development of antibiotics, vaccines and laboratory-based diagnosis, gave physicians a method to fight diseases on an individual case basis. However, the sciences of epidemiology and health education brought a population-based approach to the control of diseases. When government investments were devoted to public health infrastructure development, state and local health departments were formed to deliver the advances in microbiological technology on a population-wide basis.

One of the first actions of the Michigan State Commission of Health in 1919 was to establish a laboratory to provide outbreak investigation support. The role of the public health laboratory in Michigan evolved with laboratory science, epidemiology, changing characteristics of the state's population and the public

expectations. The public health laboratory has played an essential role in the public health accomplishments of the last century. Some, but certainly not all, of the ways public health laboratories have contributed to the ten accomplishments listed by CDC include the following:

Vaccines: Public health laboratories were often the site of research to develop and produce vaccines. For example, one of the first vaccines against whooping cough was developed by scientists Grace Eldering and Pearl Kendrick at the Western Michigan Division Laboratory in 1940. Now that vaccines are largely produced in the private sector, public health laboratories continue to support immunization efforts by diagnosis of vaccine-preventable diseases for case finding, investigation and monitoring disease activity.

Control of infectious diseases: The role of public health laboratories in detecting and supporting testing for disease outbreaks is implicit. Laboratory testing provides the basis for disease control activities such as rabies prevention, responses to meningococcal meningitis and tuberculosis case finding and treatment.

Safer, healthier foods: Testing of foods implicated as the vehicle of infection and providing diagnostic services to human cases was one of the first charges of the MDCH laboratory. As methods have developed, the laboratory's role has evolved as capacity has expanded. In addition to traditional microbiology, molecular biology based confirmation of epidemiological associations in cases and foods, identification of viral agents of foodborne disease and integration of technology outside microbiology are now employed by the public health laboratory to address food safety issues.

Healthier mothers and babies: Newborn screening programs were initiated in 1962 with PKU testing becoming mandatory two years later. The program now provides testing, follow-up and treatment for seven hereditary or metabolic disorders. It annually identifies about 150 babies, who without intervention would develop a spectrum of health problems ranging from developmental delays to death. The MDCH laboratory played a major role in prevention of birth defects by being the site of the first isolation of the rubella virus. This also played a role in vaccine development.

Fluoridation of drinking water: The safety and efficacy of fluoridation is part of an overall assurance of safe and abundant foods. Public health laboratories throughout Michigan provide water testing to assure the safety of drinking water.

Looking at accomplishments is useful to gauge how far we have come. Looking at current and future challenges is essential in determining where we need to go and how best to get there. Emerging issues for public health laboratories for the next 99 years will include addressing environmental health risks, defining the role of genetic testing in public health practice, elucidating the role of infectious agents in chronic diseases, utilization of informatics to improve laboratory practice and disease surveillance, monitoring emergence of antimicrobial resistance and development of emergency response capacity (e.g., bioterrorism response). Addressing emerging issues while remaining vigilant in areas of past gains may be the greatest challenge. As CDC concludes, the public health response is actually a complex partnership between local, state and federal governments with the medical, academia, nongovernmental agencies and the community. Success of the public health laboratory in the next century will depend on the ability to change and meet new threats as they emerge.

**10 Great Public Health Achievements –
United States, 1900-1999***

- Vaccination
- Motor-vehicle safety
- Safer workplaces
- Control of infectious diseases
- Decline of deaths for coronary heart disease and stroke
- Safer and healthier foods
- Healthier mothers and babies
- Family planning
- Fluoridation of drinking water
- Recognition of tobacco use as a health hazard

* MMWR, December 24, 1999, Vol. 48, No. 50, U.S. Department of Health and Human Services.

Detection of Norwalk-like Virus by Polymerase Chain Reaction and Electron Microscopy

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Director, Molecular Biology Section

The molecular biology and virology sections of MDCH offer reverse transcriptase polymerase chain reaction (RT-PCR) and electron microscopy (EM) testing of stool samples collected from individuals suspected of being associated with outbreaks of viral gastroenteritis. RT-PCR will specifically identify both Norwalk virus and Norwalk-like agents (NLV) (Genogroup I and Genogroup II). Methods are currently under development to allow detection of additional Norwalk-like agents, Sapporo-like viruses (Genogroup III). Sufficient genetic variability exists among the various NLV agents that RT-PCR will not detect all strains.

MDCH has developed and implemented an EM procedure to directly visualize the presence of NLV based upon their characteristic morphology. The major types of gastroenteritis viruses seen by EM include rotaviruses, enteric adenoviruses, small round viruses (structured, SRSV, and featureless, SRV) and coronaviruses. SRSVs include Norwalk-like agents, calicivirus and astrovirus. SRVs include small particles associated with SRSVs, enterovirus, parvovirus and parvovirus-like agents.

Upon identification of a suspected foodborne outbreak of gastroenteritis, the local health department is requested to contact the MDCH Bureau of Epidemiology, Division of Communicable Disease and Immunization (517-335-8165). Stool samples will be requested for bacterial or viral laboratory analysis based on the clinical history. Stool samples for bacterial analysis must be collected in Cary Blair fecal transport media while samples for viral analysis are to be collected in containers that do not contain preservatives.

When there is a strong suspicion of a viral etiology for an outbreak, the molecular biology section will perform Norwalk-like Virus RT-PCR upon receipt of the stool specimens into the laboratory, prior to the completion of bacterial analysis. In situations where a viral etiology is not strongly suspected, RT-PCR will be performed only when a bacterial pathogen is not identified and the Bureau of Epidemiology makes a subsequent request for PCR analysis. Stool samples from a suspected outbreak of viral gastroenteritis will be further analyzed by EM, when viral RNA has not been detected by the RT-PCR method. The presence of morphologically identifiable SRSV, even though NLV viral RNA may be undetectable, will support the association of NLV with the suspected outbreak.

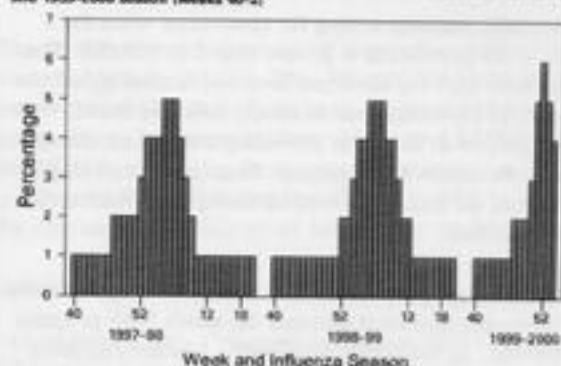
Please contact either the molecular biology section at 517-335-8850 or the virology section at 517-335-8102 with any questions regarding laboratory analysis for viral gastroenteritis.

Influenza Update 1999-2000 Season

Patty Clark, MPH
Viral Serology/Viral Isolation Unit

This season's influenza activity in the United States began to increase in mid-December, approximately four weeks earlier than the 1997-98 season and seven to eight weeks earlier than the 1998-99 season.¹ Peak influenza season this year, as measured by the percentage of patient visits to sentinel physicians for influenza-like illness, occurred during the week ending January

Percentage of patient visits to sentinel physicians for influenza-like illness,* by week of report — United States, 1997-98 and 1998-99 seasons (weeks 40-20) and 1999-2000 season (weeks 40-2)



*Defined as temperature $\geq 100^{\circ}\text{F}$ ($\geq 37.8^{\circ}\text{C}$) plus either cough or sore throat.

1.

The predominant viruses isolated this season have been influenza type A (H3N2). CDC has antigenically characterized influenza viruses received from U.S. laboratories since the beginning of the influenza season. Of all the influenza A (H3N2) viruses tested, 90 percent were similar to the vaccine strain A/Sydney/05/97.¹ This virus has been circulating in the United States for the last two influenza seasons and is well-matched to this season's vaccine.

Influenza activity continues to decline nationwide. During the week ending February 5, only eight states reported widespread influenza activity, 17 (including Michigan) reported regional activity, 21 states reported sporadic activity with four states not reporting.

Weekly Influenza Activity Estimates Reported by State & Territorial Epidemiologists
Week ending February 5, 2000 - Week 5



This season, the virology laboratory at MDCH has isolated 42 influenza viruses from patient samples submitted by physicians or health agencies throughout the state. All influenza viruses isolated have been type A (H3N2). Patients with positive cultures range in age from 2 to 78 years.

¹CDC. Update: Influenza Activity - United States, 1999-2000 Season. MMWR January 28, 2000 / 49(03): 53-57.

PULSENET UPDATE

Stephen Dietrich, M.S.
Molecular Biology Section

PulseNet is a national network of public health laboratories, the USDA and FDA. It was established by CDC to perform DNA fingerprinting on isolates of foodborne bacterial pathogens. The current method of fingerprinting used is pulsed field gel electrophoresis (PFGE). The purpose of PulseNet is to detect outbreaks through PFGE surveillance of selected pathogens and to assist investigations of outbreaks of other pathogens by allowing comparison of isolates from multiple states. The molecular biology section of MDCH began participating in PulseNet in 1999. PFGE is performed on all isolates of *Salmonella* spp. sero. typhimurium, *Shigella sonnei*, *Escherichia coli* O157:H7, and *Listeria monocytogenes* submitted to MDCH. PFGE activities in 1999 included:

Salmonella spp. sero. typhimurium: PFGE was performed on 248 isolates, 75 percent of which were in 28 clusters. None of the cases were involved in any known outbreaks. PFGE patterns commonly associated with the multiresistant DT104 strain were found in 18 percent of the cases.

S. sonnei: PFGE was performed on 431 isolates. A significant increase in cases occurred throughout 1999, doubling each quarter. One PFGE pattern was associated with 56 percent of the cases and another with 17 percent. Ninety-three percent of the cases were found in 19 clusters. Investigations are underway to find possible links between the cases in the largest cluster.

E. coli O157:H7: PFGE was performed on 88 isolates, 56 percent of which were in 14 clusters. One outbreak at a daycare was identified.

L. monocytogenes: PFGE was performed on isolates from 26 human cases and nine food items. Of the human cases, 54 percent were found in four clusters.

This technology has allowed MDCH to identify outbreaks earlier and more easily. It has also improved the epidemiological investigation of those outbreaks.

The success of PulseNet depends on the submission of all isolates of *Salmonella* spp., *Shigella* spp., enterohemorrhagic *E. coli* and *L. monocytogenes* to MDCH. MDCH would like to encourage labs to continue to submit isolates.

The Role of the Laboratory in Newborn Screening Programs

American Public Health Association
Condensed by Jacqueline Scott, D.V.M., Ph.D.
Director, Division of Chemistry and Toxicology

Over the last 40 years, Newborn Screening (NBS) programs have become well established in every state health agency and are effective at preventing disease and disability from inherited metabolic and genetic disorders. NBS programs provide or oversee medical intervention based on the results of laboratory tests performed on dried blood spots from newborn infants. Michigan's NBS program began in 1962 with screening for phenylketonuria (PKU) and has expanded to include testing for hypothyroidism, sickle cell anemia, biotinidase deficiency, maple syrup urine disease (MSUD), galactosemia and congenital adrenal hyperplasia (CAH).

NBS programs have been demonstrated to work best as centralized systems within the state public health agency, overseen and operated by dedicated public health professionals. The laboratories performing newborn screening tests are a fully integrated part of this system. The laboratory fulfills additional roles, such as training hospital staff in specimen collection which ensures accuracy of test results. Most importantly, the laboratory makes absolutely certain that abnormal results are conveyed to the medical professional who can intervene to change the affected child's life.

Initially programs were decentralized, with hospital-collected samples being sent to multiple laboratories and the test results returned for physicians to interpret and diagnose. As babies with identifiable disorders were missed due to the fragmentation of that process, states consolidated their NBS into a centralized program within the health agency. At the turn of the century, a complete NBS program involves sample collection and submission, laboratory analysis and reporting, follow-up of abnormal or incomplete results and confirmation of diagnosis and prompt implementation of necessary treatment. NBS programs also assure long term follow-up and make continuing medical advice available.

Laboratory testing is a vital component of NBS programs; mistakes can be lethal. Abnormal test results are immediately reported to the person who can assure intervention. Since mothers' hospital stays have been minimized, the NBS program staff must sometimes track down the mother and child. A confirmatory test will always be performed when an abnormal result appears, although intervention may be initiated before confirmation.

Because some disorders begin damaging the infant within the first few days of life, it is crucial that medical interventions be initiated promptly. Chronic illness, physical disability, mental retardation or death may result from delay.

The birthing hospital, the attending physician, the NBS program staff, and the laboratory must interact seamlessly to avoid those consequences.

Newborn screening programs are typically implemented when 1) the disease is a serious well-defined disorder 2) a reliable laboratory screening test is available for the newborn period 3) a reasonable cost is associated 4) effective treatment is available for the newborn once diagnosed; and 5) medical facilities to confirm the diagnosis and provide medical management and treatment are readily available. Sampling is performed before the infant leaves the hospital. It is commonly recommended that if the baby is less than 24 hours of age, another sample be obtained and tested a few weeks later as some disorders do not manifest immediately.

States generally mandate testing for syndromes when the incidence in the population is greater than 1 in 100,000. The laboratory tests look for abnormal levels of normal blood components or biomarkers not normally found in blood. Treatment may be as simple as providing a modified diet and monitoring the child's development. Mandatory screening is not considered for diseases where no therapeutic intervention has been identified.

Many state NBS programs have Newborn Screening Advisory Boards to recommend what diseases the state's NBS program should include. In Michigan, the Genetic Disease Advisory Committee (GDAC), which is comprised of medical experts including pediatric geneticists, endocrinologists and pediatricians, is the advisory body for the department. State mandates, such as in Michigan, generally derive from advisory board recommendations.

Fees charged for newborn screening services support the entire NBS program, from the cost of testing and laboratory expertise, follow-up program staff, medical management, education, as well as treatment materials (e.g., special formula). Such a fee-based program ensures that newborns are protected from shifting priorities and budget appropriations.

Because the number of laboratories performing NBS testing is limited, proficiency testing samples are not commercially available. For this reason, the National Center for Environmental Health's Division of Laboratory Sciences at CDC operates the Newborn Screening Quality Assurance Program (NBSQAP). This program provides proficiency testing samples for laboratories performing NBS testing. NBSQAP is an essential resource providing consultation and on-site assistance in resolving difficult analytical problems.

The laboratory provides resources and quality assurance both before and after the analytical stages of testing. The laboratory role includes services such as sample collection, ensuring adherence to strict turnaround times and, when needed, arranging for sample transport from inaccessible areas.

Public health laboratories provide training for hospital nurses in sample collection as proper collection is critical. If the blood spot is not of proper size and placement on the filter paper, the analytical sample may not contain the correct quantity of blood. In addition to reporting the test results the lab must address retention and storage of both samples and test results. Due to liability concerns, test records may be retained for more than 21 years.

NBS programs in the United States have allowed thousands of children to grow up healthy and lead normal lives, children who otherwise would have required chronic care if they had survived. In Colorado, identifying each child with PKU costs about \$45,000; providing this child with special formula costs between \$2,000 and \$10,000 per year more than the normal costs of child rearing¹.

The state then avoids the costs of supportive services and custodial care during ages 20 to 40 years due to the inevitable mental retardation that would have occurred without intervention. In Colorado, these would total \$3,000,000 to \$6,000,000; in Illinois, these costs are estimated at \$75,000 per year², or \$1,500,000 during that 20-year period. In Michigan, the cost savings is millions of dollars over the life of the child.

References

¹ Carol Greene, MD, Congressional Fellow, Staff to Senator Edward M. Kennedy (D-MA), as presented to the Second National Conference on Genetics and Disease Prevention, December 6, 1999, Baltimore, MD.

² Personal communication, David Carpenter, Ph.D., Chief, Division of Laboratories, IL Department of Public Health.

New Employees, Transfers and Promotions

The Bureau of Laboratories would like to welcome Martin Seling and Dave Elliot to the newborn screening section. Both come to MDCH from BioPort. Daniel Freeman has transferred from the virology section to the microbiology section.

Hao Trinh and Shirley Washington, of the microbiology section, have been promoted to senior level technicians.

David Dixon, Ph.D., has joined the MDCH UP laboratory in Houghton as a microbiologist. Dixon, with a doctorate in molecular biology, comes to the department from Michigan Technological University.

Neisseria meningitidis in Michigan

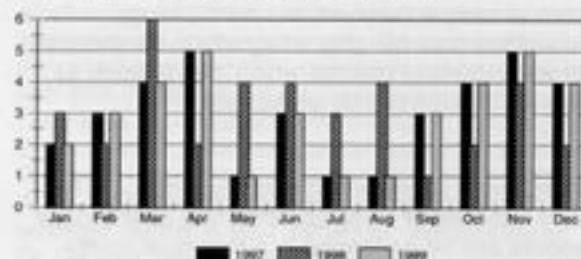
William Schneider
Enteric/STD/Chromatography Unit

Meningitis caused by *Neisseria meningitidis* is often in the news as it frequently afflicts young, apparently healthy individuals with a debilitating, sometimes fatal, disease. Carrier prevalence as high as 25% or more¹ may exist without manifestation of disease. Meningococcal meningitis is transmitted by direct contact (including respiratory droplets) from infected individuals. This disease is most prevalent among individuals newly grouped together and often in crowded conditions. Thus, outbreaks have particularly affected school and college age individuals.

The MDCH microbiology laboratory performs serotyping on all *N. meningitidis* cultures isolated from normally sterile sites, i.e. blood or spinal fluid. Serotyping will also be done on cultures isolated from the female genital tract if the colonies are smooth and typable. Rough, untypable isolates are generally considered non-invasive. Over the last three years, MDCH has identified Group B, C and Y and a few f W135 isolates. Groups B and C have historically been the most common, however Michigan, like much of the rest of the country, has seen an increase in the prevalence of Group Y isolates.

Group	B	C	Y	W135
1997	11	14	18	0
1998	11	9	15	2
1999	10	13	12	1

The incidence of meningitis due to *N. meningitidis* is expected to roughly follow the normal influenza season. Our data seems to suggest peaks in late fall to early winter and then again in the early spring. Please continue to send all *N. meningitidis* isolates from blood or spinal fluid to MDCH. This will allow for continued study of the epidemiology of this disease in Michigan.



¹Chin, James. 2000. Control of Communicable Diseases Manual, 17th Ed. American Public Health Association, Washington, D.C.

Quirky Bugs . . .

Sandip Shah, MS, MT(ASCP)

Supervisor, Reference Bacteriology

Biological Warfare: THE ANTHRAX THREAT

Imagine. It is 5:00 p.m. in Lansing on a cold and snowy day. Most microbiologists at MDCH are headed home after a busy day but a few are still struggling to finish up their work. Suddenly the phone rings.

FBI agents will be arriving soon with samples from a possible crime scene, some kind of bioterrorism threat or event. The mood changes abruptly. A couple of my colleagues and I begin collecting the needed supplies and media for the incoming samples.

Then the specimens arrive. They are worked up very carefully in a biosafety level 3 facility with FBI agents and others watching through the glass window. Everything is carefully documented, labeled and preserved as forensic evidence.

Stuff for a novel? Or some scenes from a science fiction movie? Hardly! The above scenario has occurred at MDCH. All of the events, fortunately, have turned out to be hoaxes. These valuable experiences have helped prepare us to deal with such threats. The experts in the field of biological warfare predict that it is only a matter of time before a real event will occur, most likely when we least expect it. Our only option is to be well prepared and ready at all times.

The role of the laboratory

The microbiology laboratory will play a critical role in management of a bioterrorism event. In the event of an announced attack, the microbiology laboratory can aid in the rapid diagnosis of possible cases of disease. By continuous awareness of the potential for anthrax in any clinical sample received, the microbiology laboratory also can play a key role in the detection of unannounced attacks, which may present as illness or death of unknown origin.

Handling of samples and decontamination. The safe handling of samples containing *B. anthracis* spores can be performed in a biological safety cabinet (BSC). In those cases where a BSC is not available, liquid or solid specimens that are not a fine powder, can be cultured on an open bench with minimal risk by an experienced

microbiologist. Specimen handling should always be performed while wearing latex gloves or a suitable alternative (for those with latex hypersensitivity) and lab coats or disposable protective garments. Commercially available household bleach solutions contain 5.25 percent hypochlorite and, when diluted 1:10, are effective in routine decontamination of surfaces and instruments after working with *B. anthracis*. Contaminated items such as pipettes, needles, loops and microscope slides should be immersed overnight in decontamination solution prior to autoclaving. Work surfaces should be wiped down after use with decontamination solution.

Laboratory Levels and Procedures

The Level A laboratories, composed of hospital and community microbiology laboratories, are designed to presumptively identify *B. anthracis* isolates from clinical specimens. The purpose is to obtain appropriate specimens for culture and rapid detection of *B. anthracis* from clinical specimens. Any positive smear or culture result must be promptly reported to the patient's physician and the state or local health department. It must be immediately forwarded to the nearest Level B laboratory for confirmation. In Michigan, this will be the nearest regional public health laboratory.

Level A procedures should be performed in microbiology laboratories that utilize Biosafety Level 2 practices. Laboratory coats and gloves should be worn when processing specimens and performing tests. Safety glasses or eye shields are recommended. Eating, drinking, smoking or applying makeup are prohibited. Hands must be washed prior to leaving the laboratory. Areas of the skin known to have come in contact with *B. anthracis* may be decontaminated with 0.5 percent sodium hypochlorite with a 1-minute contact time. Anthrax vaccination is not required.

Suspect laboratory findings include:

1. If a gram positive, broad, spore-containing rod is isolated, suspect *Bacillus* species.
2. If spores are not swollen, are oval shaped and the colonies have a ground glass appearance on sheep blood agar, suspect *Bacillus* morphology group 1 (includes *B. anthracis*, *B. cereus*, *B. thuringiensis*, and *B. cereus* var. *mycoides*)
3. If the isolate is nonmotile, suspect *B. anthracis* or *B. cereus* var. *mycoides*
4. If the isolate is nonhemolytic, susceptible to penicillin and has a capsule, presume it is *B. anthracis* and forward it to a Level B laboratory. Consult with a Level B Laboratory as soon as *B. anthracis* is suspected.

The Level B & C laboratory procedures will provide rapid confirmation of presumptively identified *B. anthracis* isolates. Laboratories that perform these procedures should also be proficient in Level A procedures for isolating *B. anthracis* and presumptively identifying it. Confirmatory tests for identification of *B. anthracis* include lysis by gamma phage, capsule production and direct fluorescence antibody assays. Vaccination of personnel is not required.

Level D laboratories (CDC) serve as national and international resources for the development and evaluation of new technologies for the laboratory diagnosis and epidemiologic investigation of anthrax. These laboratories create and maintain collections of reference isolates, clinical and environmental isolates and patient and environmental specimens for research and development. Personnel should be trained in the safe handling of potentially high risk samples. Vaccination of personnel is recommended.

References:

1. CDC/APHL. Laboratory Protocols for Bioterrorism Response Laboratories, 1999.
2. CDC/FDA. Biological Warfare and Terrorism, The Military and Public Health Response, 1999.

For more information visit <http://www.cdc.gov>

Surveillance for Lyme Disease

Barbara Robinson-Dunn, Ph.D.
Microbiology Section

Since 1991, MDCH has conducted active surveillance for suspect acute cases of Lyme disease in Michigan residents. The surveillance has been done in a number of different venues such as:

1. Requiring the reporting of cases of Lyme disease in Michigan under the communicable disease rules of the state
2. Stimulating the reporting of Lyme disease cases by working actively in the field with local public health departments and by thorough follow-up of reported cases to determine if they fit the national case definition
3. Provide tick identification services at no charge
4. Provide Lyme disease testing on human specimens submitted from the patient's physician
5. Providing scientific information on Lyme disease to Michigan's physicians, veterinarians and local health department personnel. Lyme disease information is also available to the non-medical citizens of Michigan
6. Assisted the Department of Natural Resources with tick surveillance in the white-tail deer population

The CDC recommends that serologic testing for Lyme disease be performed by the two-step method. MDCH provides this testing, along with culture of skin biopsies taken from characteristic erythema migrans lesions. Both forms of testing are available to Michigan residents at no charge through a patient's personal physician. You will soon be receiving a notice inquiring whether you would like to maintain a small supply of BSK II medium, used to culture for Lyme disease, in your laboratory. By returning this very short questionnaire, your facility will be supplied with BSK II and instructions for its use should the need arise. For additional information on culturing for Lyme disease, please contact Dr. Barbara Robinson-Dunn at 517-335-8067 or Susan Shiflett at 517-335-9763. If you have questions on procedures for serologic testing, please contact Dr. Jeff Massey or Dr. Dwayne Newton at 517-335-8100.

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